IPAC

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Via email: www.fda.gov/dockets/ecomments

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 2007N-0262/RIN 0910-AF92
Use of Ozone-Depleting Substances; Removal of Essential-Use Designation (Epinephrine)

Dear Sir or Madam,

These comments are submitted on behalf of the International Pharmaceutical Aerosol Consortium (IPAC) on FDA's ***Proposed Rule on Use of Ozone-Depleting Substances; Removal of Essential-Use Designation (Epinephrine).***

IPAC is an association of companies that manufacture medicines for the treatment of respiratory illnesses, such as asthma and chronic obstructive pulmonary disease (COPD). IPAC is firmly committed to the transition from CFC metered-dose inhalers (MDIs) to CFC-free alternatives, pursuant to the Montreal Protocol, and has actively engaged in the transition process in the United States. IPAC's member companies have invested, and continue to invest, substantial resources to develop CFC-free alternatives in order to accomplish the phase-out of CFC-based MDIs.

As highlighted below, IPAC believes that many of the comments it submitted in connection with the FDA rulemaking on the seven other CFC-based MDIs marketed in the United States ("the 7-moiety rule") are relevant to FDA's consideration of the phase-out of epinephrine CFC MDIs. For ease of reference, a copy of IPAC's September 10 submission is attached hereto.

In the proposed rule, FDA notes that based upon its experience with reformulation efforts for CFC-based MDIs, "it seems highly unlikely that a non-ODS inhaled epinephrine drug product will be developed and clinically tested until well after 2011."[1] In addition, FDA concludes that no technical barriers exist to reformulating CFC-based epinephrine MDIs into CFC-free products. These are important conclusions and for patient health reasons, as well as critical policy considerations, it is important to begin planning immediately to transition patients to the available CFC-free alternatives.

IPAC wishes to highlight the following additional points:

- The United States is in the final phase of accomplishing the transition to CFC-free products. As detailed in IPAC's September 10 submission to FDA, efforts to research and develop CFC-free replacements should be well-advanced at this late stage. In the context of the 7-moiety rule, IPAC recommended that effective management of this final phase of the MDI transition could require some flexibility for a seamless transition of CFC MDIs for which a CFC-free replacement is on track to generate a near-term (end 2008) submission of a comprehensive new drug application (NDA) for the CFC-free replacement product.[2] There is no evidence in the detailed information and analysis set forth in FDA's proposed rule that epinephrine CFC MDIs fall into this narrow category. Indeed, it appears that it is critical to plan now to transition epinephrine users to CFC-free alternatives.

- MDI manufacturers have known for many years that CFC MDIs would need to be phased out. Continuing to allocate CFCs to companies that have only undertaken preliminary R&D and where there is no realistic prospect of launching a CFC-free replacement in a reasonable timeframe is wholly inconsistent with the Montreal Protocol. Further, it would send a negative signal to those manufacturers that have invested substantial resources to accomplish the Protocol's important objectives. IPAC notes FDA's discussion of the important benefit of "validat[ing] expectations that the government will protect incentives to research and develop ozone-safe technologies."[3]

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[1] 72 Fed. Reg. at 53717-18.
[2] See IPAC's September 10 submission at 2-3.
[3] 72 Fed. Reg. at 53728.

- FDA has identified two primary factors that it will evaluate in connection with the phase out of epinephrine CFC MDIs, ***i.e.,*** (i) "whether adequate time exists to provide patient education for users of OTC epinephrine" and (ii) "whether adequate production capacity and supplies are available to meet the new, presumably increased, demand for therapeutic alternatives." IPAC agrees that these are important considerations and urges FDA to be proactive in collecting relevant data regarding production capacity/supply from the manufacturers of the CFC-free alternatives.[4] In addition, we urge FDA to actively explore opportunities with both the manufacturers of the CFC epinephrine products and of the CFC-free alternatives on possible means to promote timely and effective patient education.

- IPAC fully concurs with FDA's conclusion that "the United States' ability to obtain an essential use allocation for CFCs for the manufacture of OTC epinephrine MDIs in 2010 is questionable."[5] This is an important consideration and provides a critical rationale to begin planning now to transition individuals to CFC-free products, rather than extending over lengthier timeframes with increased uncertainty and concomitant risks for patient health. Further, for the reasons set forth in its September 10 comments, IPAC does not support new production of CFCs for MDIs after 2008 absent compelling circumstances that existing stockpiles are not available.

- IPAC concurs with FDA's assessment that "[p]rescription drugs available through [patient assistance programs] can be substantially less expensive than OTC epinephrine MDIs."[6] It is important to consider patient assistance programs available for the CFC-alternatives to OTC epinephrine products and we urge FDA to be proactive in obtaining relevant information from MDI manufacturers in this regard, as needed.

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[4]IPAC understands that FDA has closely tracked the transition from CFC albuterol MDIs, including production and manufacturing capacity, and this could serve as an efficient venue for FDA to obtain relevant information. If confidential business information (CBI) is relevant, FDA should establish a mechanism to receive such information. (***See,*** IPAC's 10 September submission at 4; footnote 4.)

[5] It should be noted that the European Community and the Russian Federation – the only Parties still seeking essential use CFCs for MDIs have informed the Montreal Protocol Parties that they will not seek essential uses after 2009. ***See Decision XIX/13(4)*** (September 2007).

[6] 72 Fed. Reg. at 53728.

We appreciate your consideration of these comments.

Sincerely,

Maureen Donahue Hardwick, Esq.
Secretariat and Legal Counsel

cc: Badrul Chowdhury, MD
Robert Meyer, MD

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